AMENDMENTS

In the claims:

Please amend Claim 1 to read as follows. Please cancel Claim 2, entirely without prejudice or disclaimer. Please add Claims 5-8.

Amended Claims

1.(currently amended) An isolated nucleic acid molecule comprising ~~at least 24 contiguous bases of~~ the nucleotide sequence ~~first disclosed in the NHL sequence~~ described in SEQ ID NO: 1.

2.(cancelled)

3.(original) An isolated nucleic acid molecule according to Claim 1 wherein said nucleotide sequence is present in cDNA.

4.(original) An isolated nucleic acid molecule according to Claim 3 encoding the amino acid sequence described in SEQ ID NO:2.

5. (new) An expression vector comprising a nucleic acid sequence encoding a amino acid sequence drawn from the group consisting of SEQ ID NO: 2.

6.(new) The expression vector of claim 5 wherein said nucleic acid sequence is that of SEQ ID NO:1.

7.(new) A host cell comprising the expression vector of claim 5.

8.(new) The host cell of claim 7 wherein the nucleic acid sequence is that of SEQ ID NO:1.

RESPONSE

I. Status of the Claims

Claim 1 has been amended to more clearly claim the present invention. Claim 2 has been cancelled entirely without prejudice and without disclaimer. New claims 5-8 have been added to better claim the present invention. As a result, claims 1, 3-8 are presently pending in the case.

II. Support for the Claims

Claim 1 has been amended to more clearly claim certain aspects of the invention. Amended Claim 1 finds support throughout the specification, sequence listing and claims as originally filed, with particular support being found at least in original Claim 1 and SEQ ID NO:1.

New claims 5 and 6 has been added to more clearly claim aspects of the invention. Claims 5 and 6 find support throughout the specification, sequence listing and claims as originally filed, with particular support being found at least at or about page 14 lines, 26-33 and in original SEQ ID NOS: 1 and 2.

New claims 7 and 8 has been added to more clearly claim aspects of the invention. Claims 7 and 8 find support throughout the specification, sequence listing and claims as originally filed, with particular support being found at least at or about page 14, line 33 through page 15, line 6 and in original SEQ ID NOS: 1 and 2.

As new claims 5-8 are fully supported by the specification, sequence listing and claims as originally filed, they do not constitute new matter. Entry is therefore respectfully requested.

III. Rejection of All Claims Under 35 U.S.C. § 101

The Action rejects claims under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse.

The Action discounts many of the numerous utilities described in the specification for the lipase encoding sequences of the present invention based on the position that while credible, these utilities are not specific or substantial. While Applicants in no way agree with the Examiner's arguments, Applicants have chosen to expand on only a few of the utilities as only one is required.

Applicants respectfully submit that the legal test for utility involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some

experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Even under the newly installed utility guidelines, Applicants note that MPEP 2107 (II)(B)(1) states:

> (1) If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. (MPEP 2107 (II)(B)(1))

Applicants would first like to note that in the Action the Examiner has identified issued US Patent 6,558,936 (936) which the Action notes, in the paragraph beginning on line 7 of page 6, that "The 936 patent teaches the human nucleic acid sequence of SEQ ID NO:1 encoding the polypeptide SEQ ID NO:2 which is described as lipase polypeptide...The amino acid sequence of SEQ ID NO:2 of the instant invention differs only in one amino acid residue from that of the 936 patent." Such information clearly supports Applicants' assertions that the claimed sequences encode a novel human lipase, as clearly the presently claimed sequences represent a slight variant of the human lipase described in the 936 patent.

Additionally, Applicants note that issued U.S. Patents are presumed to be valid and to meet the requirements of 35 U.S.C. §§ 101, 102, 103 and 112, specifically, that they have utility, are novel, non-obvious, are enabled, meet the written description requirements and particularly point out and distinctly claim the invention. Therefore, the Applicants' assertion that the presently claimed sequences describe a human lipase with patentable utility is clearly supported by issued U.S. Patent 6,558,936 (copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). The issuance of this U.S. patent clearly indicates that the claimed polynucleotides have utility and that such utilities were sufficiently specific and substantial to warrant the issuance of U.S. patent and therefore clearly the presently claimed polynucleotides encode a naturally occurring novel variant of a human lipase with specific and substantial utility fully compliant with 35 U.S.C. § 101.

Applicants would first like to invite the Examiner's attention to the fact that a sequence sharing greater than 99% identity at the amino acid level with a large portion of SEQ ID NO:2 of the present invention is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as "similar to lipase, CoPL-RP2 [*Homo sapiens*] (GenBank accession number XP_058404, alignment and information provided as **Exhibit A**). This identification with regards to the function of both the protein described in XP_058404 and SEQ ID NO:2 of the present invention is further supported by analysis of the functional domains present in this protein as recognized by those of skill in the art (result provided as **Exhibit B**) that show that XP_058404 and SEQ ID NO:2 of the present invention encode a protein with lipase activity. Furthermore, the function of such lipase related proteins is known to those of skill in the art as evidence by the scientific publication: "Structure and Activity of Rat Lipase-related Protein 2" (Alain Roussel, *et al.*, J Biol Chem. **273**(48): 32121-32128:1998, provided as **Exhibit C**). Therefore, clearly, in addition to the above provided evidence that the USPTO has recognized that the claimed sequences have specific, substantial and well-established utility, is the scientific evidence that the claimed sequences encode a molecule that has a specific, substantial and well-established utility.

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation and the described publications, there can be no question that those skilled in the art would clearly believe that the molecule encoded by the sequences of the present invention have specific, substantial and well established utility. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and therefore Applicants respectfully request withdrawal of the rejection.

If, somehow, the above arguments were not deemed sufficient, it should also be noted that the rejection of the present invention due to lack of patenatable utility also runs contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to

doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA. .....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

In the present case, clearly scientific evidence supports Applicants' assertions that the sequences of the present invention encode a naturally occurring novel isoform of a human lipase on which a US Patent has been issued. Thus, the protein encoded by the claimed sequences has a specific, substantial, real world or well established utility that is recognized by those of skill in the art. The present case is thus identical to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode novel isoforms of a human lipase with greater than a 95% identity to a protein having a known function (lipase), as asserted in the specification. However, even if, *arguendo*, Applicants had failed to assert this utility, according to the guidelines "Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made"(emphasis added). Thus, the present rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should not have been made and should be withdrawn.

Even though the previous arguments are believed to be dispositive of the argument with regards to utility of the claimed sequences. Applicants note that the specification details a number of uses for the presently claimed polynucleotide sequences, among these were, use in forensic analysis (see, for example, the specification at page 3, line 11 and page 12, line 6). The specification describes polymorphisms identified in the claimed sequences (page 17, lines 9-20) "Three polymorphisms have been identified which include an A/G polymorphism at the sequence region represented by nucleotide position 1141 of, for example, SEQ ID NO:1, which can result in an ile or val at corresponding amino acid position 381 of SEQ ID NO:2, a G/A polymorphism at the region of sequence represented by nucleotide position 1144 of, for example, SEQ ID NO:1, which can result in a gly or arg at corresponding amino acid position 382 of SEQ ID NO:2 and a T/G polymorphism at the region of

sequence represented by nucleotide position 378 of, for example, SEQ ID NO:1, which can result in a silent change at corresponding amino acid position 382 of SEQ ID NO:2."

Naturally occurring genetic polymorphisms such as those described in the present specification are both the basis of, and critical to, *inter alia*, forensic genetic analysis and genetic analysis intended to resolve issues of identity and paternity. These utilities are clearly real world, given that the results of identity and paternal analysis often have great emotional and substantial economic impact. This is not a throw away utility, rather it sounds like a very substantial and real world utility. What could be more substantial and real world than the loss of an individual's freedom through incarceration and in some cases even the loss of life through execution? Yet forensic analysis based on identified polymorphisms is often used to convict or acquit in many cases. Both paternal and forensic genetic analysis is based on the use of identified polymorphisms. This is a well known and generally accepted by those of skill in the art, who would readily recognize the utility and value of any identified polymorphism. Without identified polymorphisms, one would not be able to carry out such forensic or paternal analyses. The present application has identified just such essential polymorphisms within the sequences of the present invention which identify variants of the human lipase.

As such polymorphisms have inherent value as the basis for forensic analysis, paternity identification and population biology studies, which are undoubtedly "real world" utilities, the present sequences must in themselves be useful. In and of themselves each of these polymorphisms, including the silent ones, has significant and specific utility, the specificity of this utility is only amplified by the presence of so many polymorphisms that can arise in various combinations. It is also important to note that the presence of more useful polymorphic markers for such analysis would not mean that the present sequences lack utility.

Applicants respectfully point out that those of skill in the art would readily recognize that the presently described polymorphisms, exactly as they were described in the specification as originally filed, are useful in forensic analysis, population biology and paternity analysis to specifically identify individual members of the human population based on the presence or absence of the described polymorphism. Simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain one or more of these polymorphic markers does not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. Without further experimentation those of skill

in the art would recognize the utility of the identified polymorphisms and how the asserted markers can distinguish 50% of the population in the worst case scenario. Thus the presence or the absence of a particular specific polymorphism is sufficient for use in the proposed utilities. Applicants provide the following detailed explanation. Those of skill in the art would recognize that in the worst case, least useful situation, a marker would be present in half of a population and absent from the other half. Therefore the probability of an individual having such a marker would be 1 in 2 or 50%. Using the forensic analysis scenario for example, the analysis will have removed 50% of the possible suspects from the list, as either the suspect has the identified polymorphism or not. However, if a polymorphism were present in only say 10% of the population, the probability of an individual having such a polymorphic marker would be 1 in 10 (10%) and 90% of suspects could be eliminated from investigation or prosecution based on the presence or absence of the polymorphism. Clearly eliminating 90% of the suspects is better than eliminating 50% of the suspects. That said, eliminating 50% or half of the suspects on a list is without question very useful to any investigator. To reiterate, using the polymorphic markers as described in the specification as originally field will definitely distinguish members of a population from one another. In the worst case scenario, each of these markers are useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, any allegation that the use of the presently described polymorphic markers is only potentially useful would be completely without merit, and would not support the alleged lack of utility.

Should the Examiner incorrectly conclude that as any human nucleic acid sequence that contains a naturally occurring polymorphism can be used in forensic analysis, in human paternity determinations or human population migration determinations, such utilities are generic and therefore lack substantial and specific utility. First, Applicants submit that until a specific polymorphic marker is actually described it has very limited utility in forensic analysis. Put another way, simply because there is a possibility, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a specific polymorphism is actually identified and described, such a likelihood is meaningless. The present case contains identified polymorphisms that occur in a novel isoform of human lipase. Should the Examiner consider using the information presented for the first time by Applicants in the instant specification as hindsight verification that the presently claimed sequence

would be expected to have polymorphic markers. Such a hindsight analysis based on Applicants discovery would not be proper.

Alternatively, any assumption that since any sequence containing a naturally occurring polymorphism can be used such utilities are generic and therefore lack substantial and specific utility may represent a confusion between the requirement for a specific utility, which is the proper standard for utility under 35 U.S.C. § 101, with a requirement for a unique utility. The relevant case law cited by Applicants makes it abundantly clear that the presence of other or even more useful polymorphic markers for forensic analysis does **not** mean that the present sequences lack a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Importantly, the holding in the *Carl Zeiss* case is mandatory legal authority that essentially controls the outcome of the present appeal. This case, and particularly the cited quote, directly rebuts any such argument. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system

would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

In addition to the well established utilities presented above, additional utilities for the sequences of the present invention include assessing temporal and tissue specific gene expression patterns (specification at page 7, line 5), particularly using a high throughput "chip" format (specification at page 6, line 9 through page 8). Should the Examiner wish to discount Applicants' assertions regarding such uses of the presently claimed polynucleotides on DNA chips, perhaps based on the position that such a use would allegedly be generic. As set forth in Applicants' First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described sequences which encode variants of the human lipase which also contains identified polymorphisms described above) and has been shown to be expressed in human lymph node, bone marrow, testis, thyroid, colon, uterus, placenta, mammary gland. adipose, skin, esophagus, bladder, cervix, fetal kidney, fetal lung, and 12-week embryos. Thus, Applicants have identified nucleic and amino acid sequences which encode a human lipase, which contains identified polymorphisms and a characterized tissue expression pattern.

DNA chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776 (**Exhibits D-I**, copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, like the present sequences, which encode a human lipase, have identified polymorphisms and a characterized tissue expression pattern, must have utility. The sequences of the present invention which encode variants of the human lipase, have identified polymorphisms and characterized tissue expression patterns provide specific markers for the human genome (see chromosome mapping evidence provided in the specification and below), and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Accordingly, the present sequence has a specific utility

in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful.

The Examiner is further requested to reconsider that, given the huge expense of the drug discovery process, even negative information obtained using these specific markers of expression of a human lipase provides very specific markers for the human genome and have great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of DNA gene chips, such as the presently claimed sequences encoding a human lipase isoform, must in themselves be useful. Moreover, the presently described human lipase isoform sequences provide uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304, **Exhibit J**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and

Kennedy, 2001, Science *291*:1153, **Exhibit K**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions as described in the specification. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide which encodes a human lipase isoform, a utility not shared by virtually any other nucleic acid sequence. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

The Action discounts Applicants' assertion regarding the use of the presently claimed polynucleotides for gene mapping and determining chromosome structure again based on the position that such a use would allegedly be generic and therefore fail to represent a specific and substantial utility. However, as only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences, the presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Applicants' position, the

Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

Evidence provided in **Exhibit** L supports Applicants' assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions. **Exhibit** L is the result of overlaying the sequence of SEQ ID NO:1 of the present invention and the identified human genomic sequence. By doing this one is readily able to identify the portions of the genome that encode the present invention. If these regions of the genome are non-contiguous, this is indicative of individual exons. The results of such an analysis indicates that the sequence of the present invention is encoded by greater than 12 exons spread non-contiguously along a region of human chromosome 10, which is also contained within the BAC clone AC011328.11. Thus clearly one would not simply be able to identify the more than 12 distinct protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were. Additionally, it should be noted that the human lipase is now recognized to map to the same region of human chromosome 10. This further supports Applicant's position that the sequences of the present invention encodes a human lipase isoform encoded on human chromosome 10, as was described in the specification.

In addition, among other things the mapping of the relatively few expressed human genes to a particular chromosome has long been a recognized method of identifying a genes associated with particular diseases. Furthermore, the mapping of the human chromosome is a project of such widely recognized importance by those of skill in the art and even lay people, that both the US government and private corporations have dedicated millions of dollars to such a project. One is thus forced to ask, if the mapping of human chromosomes is a throw away utility then why has the US government spent so many taxpayer dollars on this project?

Finally, with full recognition of the fact that all patent applications are examined on their own merits and that the prosecution of one patent does not effect the prosecution of another patent, *In re*

Wertheim, 541 F.2d 257, 264, 191 USPQ 90, 97 (CCPA 1976). However, the issue at hand in one of whether the fact that patents have issued recognizing the utility of an almost identical molecule confers a statutory precedent of patentability to the presently claimed compositions. Example 10 of the new Utility Guidelines suggests that this is the case. There also remains a lingering issue regarding due process and equitable treatment under the law. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides; **Exhibits M-O**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples; **Exhibit P**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy), none of which contain examples of the "real-world" utilities that the Examiner appears to desire. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants agree that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants invention to a different standard of utility appears inconsistent and inequitable, such a judgement being arbitrary and capricious, a violation of due process and equal protection under the law and cannot be maintained.

In light of the evidence presented herewith and for the many compelling reasons described above, it is clear that the present invention encodes a naturally occurring novel human lipase isoform and that the utility of such molecules are specific, substantial and credible and are well-established. Therefore, Applicants submit that the rejection of the pending claims under 35 U.S.C. § 101 has been avoided. Applicants, therefore, respectfully request withdrawal of the pending rejection of claims under 35 U.S.C. § 101.

IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action also rejects all claims under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as the present invention has been shown to have "a specific, substantial, and credible utility", as detailed in the preceding section, the rejection under 35 U.S.C. § 112, first paragraph, has been avoided. Applicants therefore request that the rejection of the pending claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claim 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects Claim 1-3 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*." *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, ... the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the ... nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

The Action, on page 3, lines 20-21, states that "Regarding claim 1 and 2, they are directed all possible nucleic acid sequences comprising 24 contagious (*contiguous*) nucleotide of SEQ ID NO:1" Applicants in no way agree, **however**, as Claim 1 has been amended to read on the full-length molecule, this rejection has been rendered moot and, therefore, Applicants respectfully request that the rejection be withdrawn.

With regards to the rejection of Claim 2, Applicants respectfully submit that Claim 2 has two limitations, the first being that molecules which encode the amino acid sequence shown in SEQ ID NO: 2; and the second being hybridization under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof and covered nucleic acid molecules must meet both conditions, not just one. Applicants submit that the nucleic acid molecules identified by the intersection of both parts of Claim 2, those that encode the amino acid sequence shown in SEQ ID NO: 2; and hybridize under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof, is a finite and well defined group, which those of skill in the art could easily identify and would know how to make and use. Therefore, Applicants respectfully submit that the rejection of Claim 2 under 35 U.S.C. § 112, first paragraph, is not proper.

However, as Claim 2 has been cancelled entirely without prejudice or disclaimer this portion of the rejection has also been rendered moot. Applicants therefore respectfully request that the rejection be withdrawn.

VI. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action also rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 24 contiguous nucleotides of SEQ ID NO:1. Applicants respectfully disagree.

The Action expresses the opinion that the Claims are not enabled because "the skilled artisan would not know how to use any polynucleotide comprising as least 24 nucleotides of SEQ ID NO:1 absent undue experimentation, because the lack of functional and structural characteristics of said polynucleotides makes the probability of success in obtaining the claimed invention very low (the Action at page 4). Applicants point out that the above comment is **completely irrelevant** to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. There is absolutely **no** requirement that all species of an invention must have all of the exact same properties. It is well established that the enablement requirement is met if **any** use of the invention (or in this case, certain species of the invention) is provided (*In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka*, 224 USPQ 739 (Fed. Cir. 1985)). "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Thus, the § 112 requirement has certainly been met.

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. As discussed *In re Brana,* 34 USPQ2d 1436 (Fed. Cir. 1995; "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the

law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442.

The Examiner cites *In re Wands* (8 USPQ 2d 1400 (Fed. Cir. 1988); "*Wands*") for the proposition that the present invention could not be practiced without "undue experimentation". However, it is important to remember that in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). In *Wands*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

> Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

Wands at 1400. Thus, the need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin*, *supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants additionally point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides and DNA chips, as described in Section III, above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full-length DNA sequences, as described

in the Section responding to the Utility rejection above) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re*

Wands, supra. In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

However, as Claim 1 has been amended to read on the full-length molecule and Claim 2 has been cancelled entirely without prejudice or disclaimer, this rejection has been rendered moot. Applicants therefore respectfully request that the rejection be withdrawn.

VII. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action rejects Claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention. Applicants in no way agree, however, as Claim 2 has been cancelled entirely without prejudice or disclaimer this rejection has also been rendered moot and should therefore be withdrawn.

VIII. Rejection of Claims 1-4 Under 35 U.S.C. § 102(e)

The Action further rejects claims 1-4 under 35 U.S.C. § 102(e) as allegedly being potentially anticipated by Guegler, *et al.* (US 2002/0052034 A1) should it be issued. Applicants note that the application of Guegler, *et al.* claims priority to provisional application U.S. Serial No. 60/235,925, filed Sep. 28, 2000. This rejection depends on both the issuance of this application and whether or not the full-sequence of SEQ ID NO:2 appears in the provisional application in its entirety, which, Applicants have no way of accessing, as they do not have access to the provisional application.

The Action further rejects claims 1-4 under 35 U.S.C. § 102(e) as allegedly being potentially anticipated by Khodadoust, *et al.* (U.S. Patent 6,558,936). However, as noted by the Examiner in the Action, the amino acid sequence disclosed in U.S. Patent 6,558,936 differs from the presently claimed SEQ ID NO:2 by one amino acid. Thus, Khodadoust, *et al.* (U.S. Patent 6,558,936) does not

properly anticipate the full-length molecules claimed in the amended claims of the present invention in their entirety.

IX. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Nashed have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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Date

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